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  15mar02 08:18:42 User208669 Session D1980.1
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  $0.35  Estimated cost File1
  $0.35  Estimated cost this search
  $0.35  Estimated total session cost   0.101 DialUnits

File 155:MEDLINE(R)  1966-2002/Mar W2

    Set  Items  Description
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S1 1422429  PY>1998
S2  102572  HIV
S3     130  PRIME AND BOOST
S4     130  PRIME AND BOOST
S5      18  S2 AND S3 NOT S1
? t s5/7/1-4
 5/7/1
DIALOG(R)File 155:MEDLINE(R)
09978522   99030123   PMID: 9814958
 Prime-boost immunization strategies against HIV.
 Barnett SW; Klinger JM; Doe B; Walker CM; Hansen L; Duliege AM; Sinangil
FM
 Chiron Corporation, Emeryville, California 94608, USA.
 AIDS research and human retroviruses (UNITED STATES)  Oct 1998, 14
Suppl 3  pS299-309, ISSN 0889-2229  Journal Code: ART
 Languages: ENGLISH
 Document type: Journal Article; Review; Review, Academic
 Record type: Completed
 (106 Refs.)
 Record Date Created: 19990111

 5/7/2
DIALOG(R)File 155:MEDLINE(R)
09978521   99030122   PMID: 9814957
 Canarypox virus-based vaccines: prime-boost strategies to induce
cell-mediated and humoral immunity against HIV.
 Tartaglia J; Excler JL; El Habib R; Limbach K; Meignier B; Plotkin S;
Klein M
 Virogenetics Corporation, Troy, New York 12180, USA.
 AIDS research and human retroviruses (UNITED STATES)  Oct 1998, 14
Suppl 3  pS291-8, ISSN 0889-2229  Journal Code: ART
 Languages: ENGLISH
 Document type: Journal Article; Review; Review, Tutorial
 Record type: Completed
 (58 Refs.)
 Record Date Created: 19990111

 5/7/3
DIALOG(R)File 155:MEDLINE(R)
09723995   98206876   PMID: 9546799
 An experimental prime-boost regimen leading to HIV type 1-specific
mucosal and systemic immunity in BALB/c mice.
 Bruhl P; Kerschbaum A; Eibl MM; Mannhalter JW
 Department of Immunological Research, Immuno AG, Vienna, Austria.
 AIDS research and human retroviruses (UNITED STATES)  Mar 20 1998, 14
(5)  p401-7, ISSN 0889-2229  Journal Code: ART
 Languages: ENGLISH
 Document type: Journal Article
 Record type: Completed
 Induction of mucosal as well as systemic immunity to HIV-1 is considered
to have high priority in current concepts of future AIDS vaccines. Here we
show that the desired immune responses can be elicited by an experimental
prime-boost regimen consisting of mucosal (intragastric) application of a
recombinant vaccinia virus carrying the HIV-1 env gene (vSC25), followed by
parenteral (intradermal) immunization with the recombinant HIV-1
glycoprotein 160 (rgp160). Following intragastric immunization of mice with
vSC25 in combination with the mucosal adjuvant cholera toxin (CT), HIV-1
env-specific IgA was secreted by B cells of Peyer's patches and the lamina
propria. Moreover, mucosal (intragastric and intranasal) application of
vSC25 (both in presence or absence of CT) induced a long-lasting, HIV-1
env-specific systemic cytotoxic T cell response. Subsequent intradermal
boosters with rgp160 led to HIV-1-specific T cell memory and serum
antibodies.
 Record Date Created: 19980514

 5/7/4
DIALOG(R)File 155:MEDLINE(R)
09702785   98152198   PMID: 9491498
 Enhancement of MHC class I-restricted peptide-specific T cell induction
by a DNA prime/MVA boost vaccination regime.
 Hanke T; Blanchard TJ; Schneider J; Hannan CM; Becker M; Gilbert SC; Hill
AV; Smith GL; McMichael A
 Molecular Immunology Group, University of Oxford, John Radcliffe
Hospital, U.K.
 Vaccine (ENGLAND)  Mar 1998, 16 (5)  p439-45, ISSN 0264-410X
Journal Code: X6O
 Languages: ENGLISH
 Document type: Journal Article
 Record type: Completed
 Human immunodeficiency virus (HIV) vaccine candidates were previously
constructed as a string of cytotoxic T lymphocyte (CTL) epitopes delivered
and expressed using DNA and modified virus Ankara (MVA; an attenuated
vaccinia virus) vectors. These vaccines were shown to induce interferon
(IFN)-gamma-producing and cytolytic CD8+ T cells after a single vaccine
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administration In the course of this work, immunization protocols were sought which would improve the levels of induced HIV-specific T cells. It was found that previous immunological exposure to MVA reduced the efficiency of subsequent priming and boosting using the same vaccine vehicle. However, a combined regime whereby the animals were first primed with the DNA vaccine and then boosted with MVA was the most potent protocol for the induction of both interferon-gamma-producing and cytolytic T cells against two CTL epitopes simultaneously. The general applicability of this novel vaccination method for induction of major histocompatibility complex class I-restricted T cells is discussed.
Record Date Created: 19980415
? log hold
15mar02 08:27:29 User208669 Session D1980.2
$2.70 0.844 DialUnits File155
$0.00 18 Type(s) in Format 6
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$4.14 Estimated cost this search
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File 155:MEDLINE(R) 1966-2002/Mar W2

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Cost is in DialUnits
? b 50
15mar02 08:55:06 User208669 Session D1980.3
$0.24 0.076 DialUnits File155
$0.24 Estimated cost File155
$0.24 Estimated cost this search
$0.24 Estimated total session cost 0.076 DialUnits

File 50:CAB Abstracts 1972-2002/Feb
(c) 2002 CAB International
*File 50: Truncating CC codes is recommended for full retrieval.
See Help News50 for details.

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S1 344 IMPAIRED (3N) IMMUN? NOT HIV
S2 154 IMPAIRED (3N) IMMUNE
S3 40555 VETERINARY
S4 3 S1 AND S3
S5 8631 INTERFERENCE
S6 39 S3 AND S5
S7 295 IMPAIR? (3N)IMMUNE
S8 0 S3 AND S7 NOT S4
S9 1332 IMPAIR? AND IMMUNE
S10 2 S9 AND S4
S11 166 VACCINE AND INTERFERENCE
S12 2 S3 AND S11
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15mar02 09:01:30 User208669 Session D1980.4
$11.21 2.492 DialUnits File50
$0.00 190 Type(s) in Format 6
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$11.21 Estimated cost File50
$0.46 TYMNET
$11.67 Estimated cost this search
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File 50:CAB Abstracts 1972-2002/Feb
(c) 2002 CAB International
*File 50: Truncating CC codes is recommended for full retrieval.
See Help News50 for details.

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Cost is in DialUnits
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Set Items Description
S1 344 IMPAIRED (3N) IMMUN? NOT HIV
S2 154 IMPAIRED (3N) IMMUNE
S3 40555 VETERINARY
S4 3 S1 AND S3
S5 8631 INTERFERENCE
S6 39 S3 AND S5

S7 295 IMPAIR? (3N)IMMUNE
S8 0 S3 AND S7 NOT S4
S9 1332 IMPAIR? AND IMMUNE
S10 2 S9 AND S4
S11 166 VACCINE AND INTERFERENCE
S12 2 S3 AND S11
S13 124 S11 NOT MATERNAL NOT COLOSTRUM
S14 169325 VIRUS OR VIRUSES
S15 94 S13 AND S14
S16 5 FELINE(W)LEUKEMIA AND S9
S17 38 FELINE(W)LEUKEMIA AND RECOMBINANT
? t s15/7/25 30 36 43 44

15/7/25
DIALOG(R)File 50:CAB Abstracts

02750438 CAB Accession Number: 932289329
A review of feline infectious peritonitis virus: molecular biology, immunopathogenesis, clinical aspects, and vaccination.
Olsen, C. W.
Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin, 2015 Linden Drive West, Madison, WI, USA.
Veterinary Microbiology vol. 36 (1/2): p.1-37
Publication Year: 1993
ISSN: 0378-1135 --
Language: English
Document Type: Journal article
Topics covered in the review include molecular biology, replication of coronavirus, immunopathogenesis, virus interaction with macrophages, clinical symptoms and the first commercially available feline infectious peritonitis virus vaccine. 265 ref.

15/7/30
DIALOG(R)File 50:CAB Abstracts

02595225 CAB Accession Number: 922271718
Combined vaccination of cattle against FMD and rabies.
Palanisamy, R.; Ramanna, B. C.; Ananda Rao, K.; Srinivasan, V. A.
Indian Immunologicals, 11-4-657, Lakdi-ka-pul, 500 004 Hyderabad, India.
Microbiologica vol. 15 (1): p.45-50
Publication Year: 1992
ISSN: 0391-5352 --
Language: English
Document Type: Journal article
Three groups of crossbred calves from dams vaccinated against foot and mouth disease (FMD), were vaccinated with FMD vaccine only, combined FMD + rabies vaccine and rabies vaccine alone. Efficacy of the vaccines was determined by serum antibody assay at different intervals postvaccination. The immune response of animals to a single inoculation of FMD vaccine only (11 calves) as well as combined FMD + rabies vaccine (10 calves) was unsatisfactory due to maternally derived antibodies to FMD virus antigen. However, all of 8 calves inoculated with 2 doses of FMD vaccine and all of 10 calves inoculated with 2 doses of combined vaccine showed a satisfactory antibody response to FMD virus antigens in both groups of animals. Rabies antigen alone (5 calves) as well as combined FMD + rabies antigen (20 calves) induced satisfactory serum antibody titres to rabies antigen. There was no evidence of antigenic interference when the combined vaccine was used. 6 ref.

15/7/36
DIALOG(R)File 50:CAB Abstracts

02264190 CAB Accession Number: 902204936
Rabies vaccination of cats. Influence of simultaneous administration of a vaccine against feline leukaemia produced by genetic engineering.
Original Title: Vaccination antirabique du chat. Influence de l'administration simultanee d'un vaccin contre la leucose feline produit par genie genetique.
Ganiere, J. P.; Andre-Fontaine, G.; Artois, M.; Blancou, J.; Aubert, A.
E.N.V.N., Maladies Contagieuses, CP 3013, F-44087 Nantes, France.
Recueil de Medecine Veterinaire vol. 165 (10): p.835-838
Publication Year: 1989 --
Language: French Summary Language: english; spanish
Document Type: Journal article
Of 20 kittens aged 102-114 days, given adjuvanted, propiolactone-inactivated rabies vaccine, 10 received simultaneously, at a different s.c. injection site, feline oncovirus P45 protein vaccine prepared with recombinant Escherichia coli. Neutralizing antibody titration and challenge with rabies virus showed no interference with the immune response to the rabies vaccine. 13 ref.

15/7/43
DIALOG(R)File 50:CAB Abstracts

02104384 CAB Accession Number: 892286698
Studies on the development of a swine fever live vaccine. 1. Cloning and identification of a new attenuated virus.
Choi, C. U.; Lee, O. S.; Kim, Y. H.; An, S. H.; Hwang, E. K.
Vet. Res. Inst., Anyang, Korea Republic.
Research Reports of the Rural Development Administration, Veterinary, Korea Republic vol. 30 (2): p.42-48
Publication Year: 1988 --
Language: Korean Summary Language: english
Document Type: Journal article

A new attenuated swine fever virus was cloned by the terminal dilution and interference methods, and identified by neutralization with swine fever positive serum. Its characteristics were an interference effect against the cytopathic effect of western equine encephalomyelitis virus, a viral yield in some mammalian kidney cell cultures, and protection in vaccinated pigs against challenge with the virulent ALD strain. 14 ref.

15/7/44
DIALOG(R)File 50:CAB Abstracts

01987449 CAB Accession Number: 882209747
Immune response and challenge of cattle vaccinated simultaneously against rinderpest and foot-and-mouth disease.
Guillemin, F.; Mosienyane, M.; Richard, T.; Mannathoko, M.
Vaccine Inst., Private Bag 0031, Gaborone, Botswana.
Revue d'Elevage et de Medecine Veterinaire des Pays Tropicaux vol. 40 (3): p.225-229
Publication Year: 1987, publ. 1988 --
Language: English Summary Language: french; spanish
Document Type: Journal article
Of 17 adult Brahman crossbred cattle and Botswana local cattle, 11 were vaccinated simultaneously on opposite sides of the neck, subcutaneously, with Kabete O live rinderpest vaccine and ethyleneimine-inactivated SAT 1 vaccine. (Two received the rinderpest vaccine alone, and four were not vaccinated). Serological tests and, after 3 weeks, challenge with rinderpest virus or aphthovirus showed immunity to both viruses, with no sign of vaccine interference. 10 ref.

? t s17/7/10

17/7/10
DIALOG(R)File 50:CAB Abstracts

03287454 CAB Accession Number: 960106533
Applications of pox virus vectors to vaccination: an update.
Paoletti, E.
Delmar, NY 12054, USA.
Proceedings of the National Academy of Sciences of the United States of America vol. 93 (21): p.11349-11353
Publication Year: 1996
ISSN: 0027-8424 --
Language: English Summary Language: german
Document Type: Journal article
Recombinant pox viruses for vaccination against heterologous pathogens are reviewed. Amongst those generated are: (i) engineering the Copenhagen strain of vaccinia virus to express the rabies virus glycoprotein. When applied in baits, this recombinant has been shown to vaccinate the red fox in Europe and raccoons in the United States, stemming the spread of rabies virus infection in the wild; (ii) a fowlpox-based recombinant expressing the Newcastle disease virus fusion and haemagglutinin glycoproteins has been shown to protect commercial broiler fowls for their lifetime when the vaccine was administered at 1 day of age, even in the presence of maternal immunity against either the Newcastle disease virus or the pox vector; (iii) recombinants of canarypox virus, which is restricted for replication to avian species, have provided protection against rabies virus challenge in cats and dogs, against canine distemper virus, feline leukemia virus and equine influenza virus disease. In humans, canarypox virus-based recombinants expressing antigens from rabies virus, Japanese encephalitis virus, and HIV have been shown to be safe and immunogenic; (iv) A highly attenuated vaccinia derivative, NYVAC, has been engineered to express antigens from both animal and human pathogens. Safety and immunogenicity of NYVAC-based recombinants expressing the rabies virus glycoprotein, a polyprotein from Japanese encephalitis virus, and 7 antigens from Plasmodium falciparum have been demonstrated to be safe and immunogenic in early human vaccine studies. 34 ref.
? log hold
15mar02 09:13:09 User208669 Session D1980.5
$3.19 0.708 DialUnits File50
$0.00 43 Type(s) in Format 6
$12.00 6 Type(s) in Format 7
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$15.19 Estimated cost File50
$0.33 TYMNET
$15.52 Estimated cost this search
$15.52 Estimated total session cost 0.708 DialUnits
Logoff: level 02.02.11 D 09:13:09

? b 155
09may03 13:00:41 User208669 Session D2282.1
$0.29 0.083 DialUnits File1
$0.29 Estimated cost File1
$0.03 TELNET
$0.32 Estimated cost this search
$0.32 Estimated total session cost 0.083 DialUnits

File 155:MEDLINE(R) 1966-2003/May W1
(c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.

Set Items Description
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? ds
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S1 24823 ADENOVIR?
S2 12896 IMMUNOMODULAT?
S3 100 S1 AND S2
S4 67085 ADJUVANT?
S5 179 S1 AND S4
S6 69 VECTOR AND S5
S7 13897 TH1 OR TH2
S8 99 S1 AND S7
S9 4 S6 AND S8
S10 11413 IGG1 OR IGG2A
S11 46 S1 AND S10
? t s3/7/8 17
3/7/8
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
14191902 22212804 PMID: 12224514
Subversion of host defense mechanisms by adenoviruses.
Burgert H G; Ruzsics Z; Obermeier S; Hilgendorf A; Windheim M; Elsing A; et al
Max von Pettenkofer-Institut, Lehrstuhl Virologie, Genzentrum der Ludwig-Maximilians-Universitat, Feodor-Lynen-Str. 25, 81377 Munchen, Germany.
Current topics in microbiology and immunology (Germany) 2002, 269 p273-318, ISSN 0070-217X Journal Code: 0110513
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Adenoviruses (Ads) cause acute and persistent infections. Alike the much more complex herpesviruses, Ads encode numerous immunomodulatory functions. About a third of the viral genome is devoted to counteract both the innate and the adaptive antiviral immune response. Immediately upon infection, E1A blocks interferon-induced gene expression and the VA-RNA inhibits interferon-induced PKR activity. At the same time, E1A reprograms the cell for DNA synthesis and induces the intrinsic cellular apoptosis program that is interrupted by E1B/19K and E1B/55K proteins, the latter inhibits p53-mediated apoptosis. Most other viral stealth functions are encoded by a separate transcription units, E3. Several E3 products prevent death receptor-mediated apoptosis. E3/14.7K seems to interfere with the cytolytic and pro-inflammatory activities of TNF while E3/10.4K and 14.5K proteins remove Fas and TRAIL receptors from the cell surface by inducing their degradation in lysosomes. These and other functions that may afect granule-mediated cell death might drastically limit lysis by NK cells and cytotoxic T cells (CTL). Moreover, Ads interfere with recognition of infected cell by CTL. The paradigmatic E3/19K protein subverts antigen presentation by MHC class I molecules by inhibiting their transport to the cell surface. In concert, these viral countermeasures ensure prolonged survival in the infected host and, as a consequence, facilitate transmission. Elucidating the molecular mechanisms of Ad-mediated immune evasion has stimulated corresponding research on other viruses. This knowledge will also be instrumental for designing better vectors for gene therapy and vaccination, and may lead to a more rational treatment of life-threatening Ad infections, e.g. in transplantation patients. (213 Refs.)
Record Date Created: 20020912
Record Date Completed: 20021218

3/7/17
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
11885199 99327268 PMID: 10399069
Immune evasion by adenoviruses.
Mahr J A; Gooding L R
Department of Microbiology and Immunology, Emory University School of Medicine, Atlanta, Georgia 30322, USA. jmahr@emory.edu
Immunological reviews (DENMARK) Apr 1999, 168 p121-30, ISSN 0105-2896 Journal Code: 7702118
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Adenovirus is a human pathogen that infects mainly respiratory and gastrointestinal epithelia. While the pathology caused by this virus is generally not life threatening in immunocompetent individuals, there is a large literature describing its ability to establish a persistent infection. These persistent infections typically occur in apparently healthy individuals with no outward signs of disease. Such a long term and

benign interaction between virus and immune system requires adenoviruses to dampen host antiviral effector mechanisms that would otherwise eliminate the virus and cause immune-mediated pathology to the host. Adenovirus devotes a significant portion of its genome to gene products whose sole function seems to be the modulation of host immune responses. This review focuses on what is currently understood about how these immunomodulatory mechanisms work and how they might play a role in maintaining the virus in a persistent state. (122 Refs.)
Record Date Created: 19990914
Record Date Completed: 19990914
? t s6/7/26 30 38 41 56
6/7/26
DIALOG(R)File 155:MEDLINE(R)

11127323 98001376 PMID: 9343211
An adenovirus-simian immunodeficiency virus env vaccine elicits humoral, cellular, and mucosal immune responses in rhesus macaques and decreases viral burden following vaginal challenge.
Buge S L; Richardson E; Alipanah S; Markham P; Cheng S; Kalyan N; Miller C J; Lubeck M; Udem S; Eldridge J; Robert-Guroff M
Basic Research Laboratory, National Cancer Institute, Bethesda, Maryland 20892, USA.
Journal of virology (UNITED STATES) Nov 1997, 71 (11) p8531-41, ISSN 0022-538X Journal Code: 0113724
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Six female rhesus macaques were immunized orally and intranasally at 0 weeks and intratracheally at 12 weeks with an adenovirus type 5 host range mutant (Ad5hr)-simian immunodeficiency virus SIVsm env recombinant and at 24 and 36 weeks with native SIVmac251 gp120 in Syntex adjuvant. Four macaques received the Ad5hr vector and adjuvant alone; two additional controls were naive. In vivo replication of the Ad5hr wild-type and recombinant vectors occurred with detection of Ad5 DNA in stool samples and/or nasal secretions in all macaques and increases in Ad5 neutralizing antibody in 9 of 10 macaques following Ad administrations. SIV-specific neutralizing antibodies appeared after the second recombinant immunization and rose to titers > 10,000 following the second subunit boost. Immunoglobulin G (IgG) and IgA antibodies able to bind gp120 developed in nasal and rectal secretions, and SIV-specific IgGs were also observed in vaginal secretions and saliva. T-cell proliferative responses to SIV gp140 and T-helper epitopes were sporadically detected in all immunized macaques. Following vaginal challenge with SIVmac251, transient or persistent infection resulted in both immunized and control monkeys. The mean viral burden in persistently infected immunized macaques was significantly decreased in the primary infection period compared to that of control macaques. These results establish in vivo use of the Ad5hr vector, which overcomes the host range restriction of human Ads for rhesus macaques, thereby providing a new model for evaluation of Ad-based vaccines. In addition, they show that a vaccine regimen using the Ad5hr-SIV env recombinant and gp120 subunit induces strong humoral, cellular, and mucosal immunity in rhesus macaques. The reduced viral burden achieved solely with an env-based vaccine supports further development of Ad-based vaccines comprising additional viral components for immune therapy and AIDS vaccine development.
Record Date Created: 19971113
Record Date Completed: 19971113

6/7/30
DIALOG(R)File 155:MEDLINE(R)

10984232 97337359 PMID: 9194099
Sequential nucleic acid and recombinant adenovirus vaccination induces host-protective immune responses against Taenia ovis infection in sheep.
Rothel J S; Boyle D B; Both G W; Pye A D; Waterkeyn J G; Wood P R; Lightowlers M W
University of Melbourne, Molecular Parasitology Laboratory, Werribee, Victoria, Australia.
Parasite immunology (ENGLAND) May 1997, 19 (5) p221-7, ISSN 0141-9838 Journal Code: 7910948
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Sheep were immunized with a protective recombinant antigen (45W) from the cestode parasite Taenia ovis using three different vaccine delivery systems, either alone or in different combinations. The DNA encoding 45W was cloned into the expression plasmid pcDNA 3 and an ovine adenovirus to create nucleic acid and recombinant viral vector vaccines, respectively. Sheep received two vaccinations with various combinations of these two delivery systems and/or purified recombinant 45W protein in a conventional vaccine formulation containing Quil A as adjuvant (protein/Quil A vaccine). Sheep receiving two inoculations of either the nucleic acid or the recombinant adenovirus alone, demonstrated only low levels of 45W-specific antibody. However, immunization with either nucleic acid or recombinant adenovirus primed animals to mount an enhanced immune response after a subsequent vaccination with the protein/ Quil A vaccine. The most striking result was that sheep initially immunized with the nucleic acid vaccine and boosted with the recombinant adenovirus, mounted IgG1 responses > 65 fold higher than those of sheep receiving either vaccine alone. The level of antibody in these sheep was commensurate with that observed in animals vaccinated twice with the protein/Quil A adjuvanted vaccine. In both cases, host-protection from experimental challenge infection with T. ovis was

obtained.
Record Date Created: 19970814
Record Date Completed: 19970814

6/7/38
DIALOG(R)File 155:MEDLINE(R)

10220349 96021593 PMID: 7483252
Immunization trial of cats with a replication-defective adenovirus type 5 expressing the ENV gene of feline immunodeficiency virus.
Gonin P; Fournier A; Oualikene W; Moraillon A; Eloit M
Laboratoire de Genetique Moleculaire, Genetique virale, INRA, Ecole Nationale Veterinaire, Maisons Alfort, France.
Veterinary microbiology (NETHERLANDS) Aug 1995, 45 (4) p393-401, ISSN 0378-1135 Journal Code: 7705469
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Our aim was to develop a recombinant replication-defective adenovirus suitable for the vaccination of cats against feline immunodeficiency virus. We first demonstrated that this vector was able to transfer a marker gene (E. coli beta-galactosidase) in feline cells in vitro. We then constructed an adenovirus type 5 expressing the Feline Immunodeficiency Virus (FIV) envelope (ENV) gene of the Wo isolate in the absence of the rev gene (Ad-ENV-Wo). Ad-ENV-Wo was then tested in four cats in a 3 injections scheme (at day 0, day 30 and day 210). Four other control cats received Ad-gp50, a similar recombinant adenovirus expressing gp50 (Ad-gp50) of pseudorabies virus (PRV). Viruses were formulated in two different kind of oil adjuvants (water/oil and water/oil/water), a protocol previously shown to enhance the immune response against the virus-induced protein. The control cats developed neutralizing antibodies against PRV, demonstrating the potency of recombinant human adenovirus 5 (Ad5) as a vector in cats. Antibody responses appeared after the first injection and were higher with the water/oil/water formulation than with the water/oil controls. However, none of the four cats vaccinated with Ad-ENV-Wo developed antibodies against two peptides of the envelope protein. Animals were challenged with 20 infectious doses 50% of the strain Wo. All of them developed antibodies against FIV within 4 to 5 weeks, and FIV virus could be isolated from all.
Record Date Created: 19951207
Record Date Completed: 19951207

6/7/41
DIALOG(R)File 155:MEDLINE(R)

09795199 21602543 PMID: 11739678
Adenovirus hexon protein is a potent adjuvant for activation of a cellular immune response.
Molinier-Frenkel Valerie; Lengagne Renee; Gaden Florence; Hong Saw-See; Choppin Jeannine; Gahery-Segard Hanne; Boulanger Pierre; Guillet Jean-Gerard
Laboratoire d'Immunologie des Pathologies Infectieuses et Tumorales, INSERM U445, Institut Cochin de Genetique Moleculaire, Hopital Cochin, 75014 Paris, France. frenkel@cochin.inserm.fr
Journal of virology (United States) Jan 2002, 76 (1) p127-35, ISSN 0022-538X Journal Code: 0113724
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The capacity of recombinant adenoviruses (rAd) to induce immunization against their transgene products has been well documented. In the present study, we evaluated the vaccinal adjuvant role of rAd independently of its vector function. BALB/c mice received one subcutaneous injection of a mixture of six lipopeptides (LP6) used as a model immunogen, along with AdE1 degrees (10(9) particles), a first-generation rAd empty vector. Although coinjected with a suboptimal dose of lipopeptides, AdE1 degrees significantly improved the effectiveness of the vaccination, even in the absence of booster immunization. In contrast to mice that received LP6 alone or LP6 plus a mock adjuvant, mice injected with AdE1 degrees plus LP6 developed both a polyspecific T-helper type 1 response and an effector CD8 T-cell response specific to at least two class I-restricted epitopes. The helper response was still observed when immunization was performed using LP6 plus a mixture of soluble capsid components released from detergent-disrupted virions. When mice were immunized with LP6 and each individual capsid component, i.e., hexon, penton base, or fiber, the results obtained suggested that hexon protein was responsible for the adjuvant effect exerted by disrupted Ad particles on the helper response to the immunogen. Our results thus have some important implications not only in vaccinology but also for gene therapy using rAd vectors.
Record Date Created: 20011212
Record Date Completed: 20020110

6/7/56
DIALOG(R)File 155:MEDLINE(R)

09134365 20434547 PMID: 10981668
Recombinant adenoviral vectors have adjuvant activity and stimulate T cell responses against tumor cells.
Geutskens S B; van der Eb M M; Plomp A C; Jonges L E; Cramer S J; Ensink N G; Kuppen P J; Hoeben R C
Department of Molecular Cell Biology, Leiden University Medical Center, The Netherlands.
Gene therapy (ENGLAND) Aug 2000, 7 (16) p1410-6, ISSN 0969-7128

Journal Code. 9421525
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The host-immune response against adenoviruses forms a major obstacle for their use as gene therapy vectors for treatment of genetic defects. None the less, they are the preferred vectors for in vivo gene transfer in experimental gene therapy protocols for cancer. In this article we demonstrate the antitumor efficacy of adenovirus-mediated transfer of human interleukin-2 cDNA in the rat-CC531 model for hepatic metastases of colorectal cancer: intratumoral administration of 10 plaque-forming units of the hIL-2-expressing adenoviral vector, AdCAIL-2, resulted in a cessation of tumor growth in 80% of the injected tumors. In control groups receiving AdCnull, a vector with the same viral backbone, but lacking transgene expression, none of the tumors responded. However, intratumoral treatment with this vector significantly enhanced tumor regression induced by systemic IL-2 protein treatment, which was used as a positive control. In addition we show, by performing delayed-type of hypersensitivity assays, that AdCnull when injected intratumorally enhances recognition of tumor antigens by T lymphocytes to the same extent as intratumoral treatment with the IL-2-expressing vector. The replication-deficient adenoviruses appear to have a therapeutic advantage in cytokine-mediated immunotherapy: even adenovirus vectors that do not express a transgene, show adjuvant activity and stimulate an antitumor immune response.
Record Date Created: 20000926
Record Date Completed: 20000926
? t s8/7/1-4
8/7/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
14812106 22619999 PMID: 12734353
TNF Enhances CD4(+) T Cell Alloproliferation, IFN-gamma Responses, and Intestinal Graft-Versus-Host Disease by IL-12-Independent Mechanisms.
Brown Geri R; Lee Edward L; Thiele Dwain L
Division of Digestive and Liver Diseases, Department of Internal Medicine, and. Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX 75235. Dallas Veterans Affairs Medical Center, Dallas, TX 75216.
Journal of immunology (Baltimore, Md. - 1950) (United States) May 15 2003, 170 (10) p5082-8, ISSN 0022-1767 Journal Code: 2985117R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
Inhibition of TNF/TNFR2 interactions ameliorates intestinal graft-vs-host disease (GVHD) and Th1 cytokine responses induced by transfer of B6 CD4(+) spleen cells into irradiated MHC class II disparate B6.C-H-2(bm12) (bm12) x B6 F(1) recipients. The present studies examined whether these effects of TNF are IL-12 dependent. T cell proliferative responses of B6.129S1-IL-12rb2(tm1Jm) (B6.IL-12R(-/-)) responder spleen cells were found to be comparable to those of control B6 spleen cells. TNF inhibition reduced T cell proliferation and IFN-gamma production in supernatants of MLC using either B6.IL-12R(-/-) or control B6 responder cells. GVHD induced wasting disease in recipients of B6.IL-12R(-/-) CD4(+) spleen cells that received a TNF inhibitor-encoding adenovirus (5.4 +/- 6.5% weight loss (n = 7)) was significantly reduced compared with levels of weight loss observed in recipients that had received a control adenovirus (25.7 +/- 12.2% weight loss (n = 11), p = 0.001). Furthermore, TNF inhibition was associated with a reduction in colonic GVHD scores (p = 0.039) and in the percentage of the splenic CD4(+) T cells that expressed IFN-gamma (16 vs 6%). These findings indicate that TNF promotes CD4(+) T cell alloproliferation, IFN-gamma responses, and intestinal GVHD by IL-12-independent mechanisms.
Record Date Created: 20030507

8/7/2
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
14710932 22273930 PMID: 12386826
Immunosuppressive effects of interleukin-12 coexpression in melanoma antigen gene-modified dendritic cell vaccines.
Ribas Antoni; Amarnani Saral N; Buga Georgette M; Butterfield Lisa H; Dissette Vivian B; McBride William H; Glaspy John A; Ignarro Louis J; Economou James S
Department of Surgery, University of California at Los Angeles, 90095-1782, USA.
Cancer gene therapy (England) Nov 2002, 9 (11) p875-83, ISSN 0929-1903 Journal Code: 9432230
Contract/Grant No.: K12 CA76905; CA; NCI; R01 CA77623; CA; NCI; R01 CA79976; CA; NCI; T32 CA75956; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Genetic immunotherapy with tumor antigen gene-modified dendritic cells (DC) generates robust immunity, although antitumor protection is not complete in all models. Previous experience in a model in which C57BL/6 mice immunized with DC transduced with adenoviral vectors expressing MART-1 demonstrated a 20-40% complete protection to a tumor challenge with B16 melanoma cells. Tumors that did develop in immunized mice had slower growth kinetics compared to tumors implanted in naive mice. In the present study, we wished to determine if the supraphysiological production of the Th1-skewing cytokine interleukin-12 (IL-12) could enhance immune activation and antitumor protection in this model In a series of experiments

immunizing mice with DC cotransduced with MART-1 and IL-12, antitumor protection and antigen-specific splenocyte cytotoxicity and interferon gamma production inversely correlated with the amount of IL-12 produced by DC. This adverse effect of IL-12 could not be explained by a direct cytotoxic effect of natural killer cells directed towards DC, nor the production of nitric oxide leading to down-regulation of the immune response - the two mechanisms previously recognized to explain immune-suppressive effects of IL-12-based vaccine therapy. In conclusion, in this animal model, IL-12 production by gene-modified DC leads to a cytokine-induced dose-dependent inhibition of antigen-specific antitumor protection.

Record Date Created: 20021018
Record Date Completed: 20030417

8/7/3

DIALOG(R)File 155:MEDLINE(R)
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14692179 22472076 PMID: 12584217

Local delivery of adenoviral vectors encoding murine interleukin 10 induces colonic interleukin 10 production and is therapeutic for murine colitis.

Lindsay J O; Ciesielski C J; Scheinin T; Brennan F M; Hodgson H J

Kennedy Institute of Rheumatology Division, Imperial College School of Medicine, London, UK. j.lindsay@doctors.org.uk

Gut (England) Mar 2003, 52 (3) p363-9, ISSN 0017-5749 Journal Code: 2985108R

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

INTRODUCTION: Interleukin 10 knockout (IL-10-/-) mice spontaneously develop a Th1 T cell mediated colitis with many similarities to Crohn's disease. Daily injections of IL-10 are unable to induce remission in mice with established disease. In contrast, we have shown previously that intravenous administration of adenoviral vectors encoding IL-10 (AdvmuIL-10) induces hepatic IL-10 release and leads to long term disease suppression with profound systemic immunoregulatory changes. AIMS: To determine whether rectal delivery of AdvmuIL-10 induces localised colonic IL-10 expression without systemic immune suppression, and assess its therapeutic efficacy in IL-10-/- mice with established colitis. RESULTS: A single rectal infusion of 5 x 10(8) PFU AdvmuIL-10 to 10 week IL-10-/- mice resulted in a median level of 27.3 pg/mg IL-10 in colonic homogenates harvested one week later. IL-10-/- mice with established colitis treated with an enema of 5 x 10(8) PFU AdvmuIL-10 entered clinical and histological remission whereas empty cassette adenovirus (Adv0) or phosphate buffered saline (PBS) treated mice developed progressive disease. After four weeks, the histological score of AdvmuIL-10 treated mice (4.4 (1.5)) was significantly lower than that of Adv0 (11.1 (1.1); p<0.001) and PBS (10.9 (1.0); p<0.01) treated controls. In addition, the stool concentration of IL-1 beta over the four week experiment was significantly higher in mice treated with saline or Adv0 than in those treated with AdvmuIL-10 (p<0.01). CONCLUSION: Local AdvmuIL-10 therapy reverses colitis in IL-10-/- mice without the systemic effects seen after intravenous administration. Gene therapy strategies using adenoviral vectors encoding immunoregulatory cytokines may prove to be a potent approach to the treatment of chronic inflammatory diseases such as Crohn's disease.

Record Date Created: 20030213
Record Date Completed: 20030411

8/7/4

DIALOG(R)File 155:MEDLINE(R)
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14673543 22450295 PMID: 12562382

Dendritic cells infected with adenovirus expressing the thyrotrophin receptor induce Graves' hyperthyroidism in BALB/c mice.

Kita-Furuyama M; Nagayama Y; Pichurin P; McLachlan S M; Rapoport B; Eguchi K

First Department of Internal Medicine and Department of Pharmacology 1, Nagasaki University School of Medicine, Nagasaki, Japan.

Clinical and experimental immunology (England) Feb 2003, 131 (2) p234-40, ISSN 0009-9104 Journal Code: 0057202

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Dendritic cells (DCs) are the most potent antigen-presenting cells and a prerequisite for the initiation of primary immune response. This study was performed to investigate the contribution of DCs to the initiation of Graves' hyperthyroidism, an organ-specific autoimmune disease in which the thyrotrophin receptor (TSHR) is the major autoantigen. DCs were prepared from bone marrow precursor cells of BALB/c mice by culturing with granulocyte macrophage-colony stimulating factor and interleukin-4. Subcutaneous injections of DCs infected with recombinant adenovirus expressing the TSHR (but not beta-galactosidase) in syngeneic female mice induced Graves'-like hyperthyroidism (8 and 35% of mice after two and three injections, respectively) characterized by stimulating TSHR antibodies, elevated serum thyroxine levels and diffuse hyperplasitc goiter. TSHR antibodies determined by ELISA were of both IgG1 (Th2-type) and IgG2a (Th1-type) subclasses, and splenocytes from immunized mice secreted interferon-gamma (a Th1 cytokine), not interleukin-4 (a Th2 cytokine), in response to TSHR antigen. Surprisingly, IFN-gamma secretion, and induction of antibodies and disease were almost completely suppressed by co-administration of alum/pertussis toxin, a Th2-dominant adjuvant, whereas polyriboinosinic polyribocytidylic acid, a Th1-inducer, enhanced splenocyte

secretion of IFN-gamma without changing disease incidence. These observations demonstrate that DCs efficiently present the TSHR to naive T cells to induce TSHR antibodies and Graves'-like hyperthyroidism in mice. In addition, our results challenge the previous concept of Th2 dominance in Graves' hyperthyroidism and provide support for the role of Th1 immune response in disease pathogenesis.
Record Date Created: 20030203
Record Date Completed: 20030407

? t s11/7/9 15 18 19 21

11/7/9
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
11896888 99339702 PMID: 10413357
Antigen-specific cytokine and antibody isotype profiles induced by mucosal and systemic immunization with recombinant adenoviruses.
Papp Z; Babiuk L A; Baca-Estrada M E
Veterinary Infectious Disease Organization, University of Saskatchewan, Saskatoon, Canada.
Viral immunology (UNITED STATES) 1999, 12 (2) p107-16, ISSN 0882-8245 Journal Code: 8801552
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We investigated antigen-specific antibody and T-cell responses in mice immunized with human adenovirus type 5 (HAd5) vectors expressing either the authentic or truncated form of glycoprotein D (gD and tgD, respectively) of bovine herpesvirus type 1 (BHV-1). We also tested whether different routes of immunization influenced the level and type of immunity. Immunization intranasally (i.n.) stimulated higher levels of gD-specific IgA in the lung and nasal washes and induced a higher frequency of gD-specific antibody secreting cells (CSs) in the lung than did immunization subcutaneously (s.c.). In addition, immunization i.n. stimulated gD-specific systemic antibody responses of a higher IgG1/IgG2a ratio and lower numbers of gD-specific interferon (IFN)-gamma SCs in the spleen than did immunization s.c. HAd5-specific responses also depended on the route of immunization and were characterized by lower IFN-gamma interleukin (IL)-4 ratios than gD-specific responses. Immunization with the tgD-expressing vector induced generally lower antibody and cytokine responses than the gD-expressing vector. Higher numbers of antigen-specific IgA SCs in the lung as measured by enzyme-linked immunospot (ELISPOT) assay correlated with higher levels of IgA in the respiratory tract as measured by enzyme-linked immunosorbent (ELISA) assay, although there was no such correlation for IgG responses of any isotype. In conclusion, the route of immunization and form of antigen had an impact on the level and type of immune responses induced by adenovirus vectors.
Record Date Created: 19990831
Record Date Completed: 19990831

11/7/15
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
11643916 99077921 PMID: 9858523
Processing of switch transcripts is required for targeting of antibody class switch recombination.
Hein K; Lorenz M G; Siebenkotten G; Petry K; Christine R; Radbruch A
Deutsches Rheuma-Forschungszentrum Berlin, 10115 Berlin, Germany.
Journal of experimental medicine (UNITED STATES) Dec 21 1998, 188 (12) p2369-74, ISSN 0022-1007 Journal Code: 2985109R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Antibody class switching is mediated by somatic recombination between switch regions of the immunoglobulin heavy chain gene locus. Targeting of recombination to particular switch regions is strictly regulated by cytokines through the induction of switch transcripts starting 5' of the repetitive switch regions. However, switch transcription as such is not sufficient to target switch recombination. This has been shown in mutant mice, in which the I-exon and its promoter upstream of the switch region were replaced with heterologous promoters. Here we show that, in the murine germline targeted replacement of the endogenous gamma1 promoter, I-exon, and I-exon splice donor site by heterologous promoter and splice donor sites directs switch recombination in activated B lymphocytes constitutively to the gamma1 switch region. In contrast, switch recombination to IgG1 is inhibited in mutant mice, in which the replacement does not include the heterologous splice donor site. Our data unequivocally demonstrate that targeting of switch recombination to IgG1 in vivo requires processing of the Igamma1 switch transcripts. Either the processing machinery or the processed transcripts are involved in class switch recombination.
Record Date Created: 19990122
Record Date Completed: 19990122

11/7/18
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
11121203 97479812 PMID: 9339893
Comparison of various expression plasmids for the induction of immune response by DNA immunization.
Lee A H; Suh Y S; Sung J H; Yang S H; Sung Y C
Department of Life Science, School of Environmental Engineering, Pohang University of Science and Technology, Korea.
Molecules and cells (KOREA) Aug 31 1997, 7 (4) p495-501, ISSN

1016-8478 Journal Code: 9610936
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Intramuscular injection of plasmid DNA is an efficient method to introduce a foreign gene into a live animal. We investigated several factors affecting the gene transfer efficiency and the following immune response by intramuscular injection of plasmid DNA. When the strength of several highly efficient viral promoters was compared in muscle by using the chloramphenicol acetyltransferase (CAT) gene as an indicator, cytomegalovirus (CMV) immediate early promoter was found to be stronger than any other viral promoters including Rous sarcoma virus (RSV), murine leukemia virus (SL3-3) and simian virus 40 (SV40) early promoters. Inclusion of adenovirus tripartite leader (TPL) sequences and a synthetic intron in the 5' untranslated region of mRNA moderately stimulated the CAT expression. On the other hand, the expression of encephalomyocarditis virus (EMCV) VP1 gene was greatly enhanced by the TPL sequences and an intron. The level of humoral immune response by intramuscular injection of various VP1 expression plasmids was compared. The seroconversion rate was highly dependent on the strength of the expression vector. However, the ratio of IgG1 and IgG2a immune response was not significantly variable depending on the strength of the expression vector. Also, the efficiency of the sindbis virus-based DNA vector was examined for the gene expression and immune response. Although a high level of CAT expression was obtained in muscle by using this system, VP1 was not produced as much as the conventional expression vectors. Furthermore, little humoral immune response was elicited by intramuscular injection of VP1-expressing sindbis vector, suggesting that this system was not superior to the conventional vector for DNA immunization.
Record Date Created: 19971114
Record Date Completed: 19971114

11/7/19
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
11008295 97361622 PMID: 9218583
Adenoviral gene delivery elicits distinct pulmonary-associated T helper cell responses to the vector and to its transgene.
van Ginkel F W; McGhee J R; Liu C; Simecka J W; Yamamoto M; Frizzell R A; Sorscher E J; Kiyono H; Pascual D W
Department of Microbiology and The Cystic Fibrosis Research Center, University of Alabama at Birmingham, 35294, USA.
Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Jul 15 1997, 159 (2) p685-93, ISSN 0022-1767 Journal Code: 2985117R
Contract/Grant No.: AI 18958; AI; NIAID; AI 40288; AI; NIAID; CA 54430; CA; NCI; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Replication-deficient adenovirus (Ad) vectors are effective to specifically target the respiratory epithelium for either corrective gene therapy such as cystic fibrosis or for mucosal immunization. As a consequence of transducing the lower respiratory tract with an E1/E3 deleted Ad5 vector, host responses have been characterized by the duration of transgene expression and by the induction of CTL responses. However, limited emphasis has been devoted to understanding the contribution of CD4+ T cell responses to the Ad vector. Both CD4+ and CD8+ T cells migrate into the lung following sequential intratracheal Ad5 transgene instillations. Isolated CD3+ T lymphocytes from the lungs were predominantly of the Th2 type, and after cell sorting, the IL-4-producing T cells were largely CD4+, while IFN-gamma expression was associated with both CD4+ and CD8+ T cells. Ab responses to the Ad5 vector and to the expressed transgene beta-galactosidase (beta gal) revealed elevated bronchial and serum IgA and IgG Abs with low neutralization titers. Analysis of serum IgG subclass responses showed IgG1 and IgG2b with lower IgG2a Abs to Ad5 and IgG2a and IgG2b Ab responses to beta gal. Ad5-specifc CD4+ T cells produced both Th1 (IFN-gamma and IL-2)- and Th2 (IL-4, IL-5, IL-6)-type cytokines, while beta gal-specific CD4+ T cells secreted IFN-gamma and IL-6. This study provides direct evidence for the concomitant induction of Th2- with Th1-type responses in both the pulmonary systemic and mucosal immune compartments to the Ad5 vector as well as a Th1-dominant response to the transgene.
Record Date Created: 19970805
Record Date Completed: 19970805

11/7/21
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
10882740 97234531 PMID: 9079805
Humoral immune response to the capsid components of recombinant adenoviruses: routes of immunization modulate virus-induced Ig subclass shifts.
Gahery-Segard H; Juillard V; Gaston J; Lengagne R; Pavirani A; Boulanger P; Guillet J G
Laboratoire d'Immunologie des Pathologies Infectieuses et Tumorales, INSERM Unite 445, Universite R. Descartes, Paris, France. gahery@icgm.cochin.inserm.fr
European journal of immunology (GERMANY) Mar 1997, 27 (3) p653-9, ISSN 0014-2980 Journal Code: 1273201
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type Completed

This study examines in detail the capsid-specific humoral immune response of BALB/c mice after one single injection of a replication-defective adenovirus. Two routes of immunization, intravenous (i.v.) and intraperitoneal (i.p.), were compared for the response induced against the adenovirus particle and the three major components of the viral capsid, hexon, penton base, and fiber. A single immunization with the replication-defective adenovirus induces a long and persistent humoral response specific for the virus. However, the molecular components of the viral capsid are differentially recognized depending on the route of immunization. The sera from mice immunized i.p. recognized only the hexon protein and a preferential switch to the IgG2a subclass was obtained which remained stable 100 days post-immunization. The sera obtained from mice immunized i.v. gave a more complex response. At the beginning of the response, an isotype bias toward the IgG2a subclass was observed, but the isotype distribution changed during the whole period of the response. Neutralizing activity was maximum 45 days after immunization by both routes, and no activity was detectable after 3 months. However, the i.v. serum displayed a higher neutralizing activity than the i.p. serum. The IgM antiviral antibodies appeared to be an important component of the neutralizing activity, and the two routes of immunization do not induce the same IgG isotypes to neutralize viral infectivity. Extension of these findings to human gene therapy using recombinant adenoviruses may help to characterize the precise viral protein targets of neutralizing antibodies.

Record Date Created: 19970429

Record Date Completed: 19970429

? log hold

09may03 13:24:25 User208669 Session D2282.2

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$0.00 219 Type(s) in Format 6

$3.36 16 Type(s) in Format 7

$3.36 235 Types

$10.22 Estimated cost File155

$5.60 TELNET

$15.82 Estimated cost this search

$16.14 Estimated total session cost 2.227 DialUnits

Logoff: level 02.13.02 D 13:24:25

? b 155
12may03 08:54:19 User208669 Session D2284.1
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$0.29 Estimated cost File1
$0.29 Estimated cost this search
$0.29 Estimated total session cost 0.082 DialUnits

File 155:MEDLINE(R) 1966-2003/May W1
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*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.

Set Items Description
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? ds
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S1 9468 T(W)HELPER
S2 24824 ADENOVIR?
S3 3 SQ AND S2
S4 49 S1 AND S2
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4/7/5
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
14222379 22339270 PMID: 12450695
Vaccination with an adenoviral vector encoding hepatitis C virus (HCV) NS3 protein protects against infection with HCV-recombinant vaccinia virus.
Arribillaga Laura; de Cerio Ascension Lopez Diaz; Sarobe Pablo; Casares Noelia; Gorraiz Marta; Vales Africa; Bruna-Romero Oscar; Borras-Cuesta Francisco; Paranhos-Baccala Glaucia; Prieto Jesus; Ruiz Juan; Lasarte Juan Jose; et al
Department of Internal Medicine, Centro de Investigaciones Medicas Aplicadas (CIMA), University of Navarra, Pamplona, Spain. larribi@alumni.unav.es
Vaccine (Netherlands) Dec 13 2002, 21 (3-4) p202-10, ISSN 0264-410X Journal Code: 8406899
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
Cellular immune response plays an important role in the clearance of hepatitis C virus (HCV). Thus, development of efficient ways to induce anti-viral cellular immune responses is an important step toward prevention and/or treatment of HCV infection. With this aim, we have constructed a replication-deficient recombinant adenovirus expressing HCV NS3 protein (RAdNS3). The efficacy of RAdNS3 was tested in vivo by measuring the protection against infection with a recombinant vaccinia virus expressing HCV-polyprotein (vHCV1-3011). Immunisation with 10(9)pfu of RAdNS3 induced anti-NS3 humoral, T helper and T cytotoxic responses. We identified eight epitopes recognised by IFN-gamma producing cells, five of them exhibiting lytic activity. Moreover, we show that RAdNS3 immunised mice were protected against challenge with vHCV1-3011 and that this protection was mediated by CD8(+) cells. In conclusion, our results suggest that adenoviral vectors encoding NS3 might be useful for the induction of prophylactic and/or therapeutic anti-HCV immunity.
Record Date Created: 20021126

4/7/10
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
11844961 99285702 PMID: 10359207
Evaluation of cellular immune responses in rhesus monkeys subjected to adenovirus-mediated gene transfer into the cervix.
Sarkar A K; Mitchell M F; Hamada K; Buchl S J; Satterfield W C; Schapiro S J; Keeling M E; Sastry K J
Department of Veterinary Sciences, University of Texas M.D. Anderson Cancer Center, Bastrop 78602, USA.
Cancer gene therapy (ENGLAND) May-Jun 1999, 6 (3) p220-7, ISSN 0929-1903 Journal Code: 9432230
Contract/Grant No.: CA 65571; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We reported previously that direct injection of a recombinant adenovirus (rAd), Ad5CMV-beta-gal, into the cervix of the rhesus monkey resulted in efficient beta-galactosidase expression in the cervix within 3 days. In these studies, we also observed the induction of anti-adenovirus (Ad)-specific immunoglobulin G responses after 22 days. In the continuation of evaluating the anti-Ad-specific immune responses resulting from this approach of gene targeting to the cervix, we measured the cellular immune responses. The introduction of Ad5CMV-beta-gal into the cervix by direct injection, but not by the abrasion technique, resulted in the induction of strong proliferative responses against extracts of cells infected with Ad5CMV-beta-gal but not against control uninfected cells. These responses were initially detected at 22 days postinjection and coincided with the abrogation of transgene expression. Significant levels of proliferative responses were maintained for < or =83 days. Multiple injections of rAds had no significant enhancing effect on either the level or longevity of the proliferative responses. At 3 days after the injection of Ad5CMV-beta-gal, when the transgene expression in the cervix was clearly evident, proliferative responses against the rAd were not detectable. However, the production of low but significant amounts of interleukin-10, a cytokine characteristic of T helper type 2 responses that promote humoral immune

responses, was observed at the 3-day point in these animals. These results suggest that significant differences exist between the kinetics of transgene expression and the priming of specific host immune responses, and that these differences may be important for devising alternate strategies to improve techniques for Ad-mediated gene therapy of cervical cancer.
Record Date Created: 19991005
Record Date Completed: 19991005

4/7/14
DIALOG(R)File 155:MEDLINE(R)

11347727 98227917 PMID: 9568962
Immunological basis for protection in a murine model of tick-borne encephalitis by a recombinant adenovirus carrying the gene encoding the NS1 non-structural protein.
Timofeev A V; Ozherelkov S V; Pronin A V; Deeva A V; Karganova G G; Elbert L B; Stephenson J R
Chumakov Institute of Poliomyelitis and Viral Encephalitides RAMS, Moscow Region, Russia.
Journal of general virology (ENGLAND) Apr 1998, 79 (Pt 4) p689-95, ISSN 0022-1317 Journal Code: 0077340
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The humoral immune response to flaviviruses is mainly directed to the major envelope protein, E, and a glycosylated non-structural protein, NS1. Cell-mediated immune responses, however, appear to be directed mainly against non-structural proteins. Experiments described here show that a defective recombinant adenovirus (Rad51) containing the gene encoding the NS1 protein of tick-borne encephalitis virus can induce a strong protective immune response against several pathogenic tick-borne flaviviruses in an experimental animal model, and can enhance the efficacy of conventional vaccine preparations. A protective immune response against a lethal virus challenge can also be induced by the passive transfer of antibodies, B cells or T cells from animals vaccinated with Rad51. Raised levels of non-neutralizing antibodies and cytokines associated with a T helper cell-type 1 immune response are also observed. These data demonstrate the importance of non-structural viral proteins in the protective immune response against flaviviruses and support the use of non-structural viral proteins as vaccine components.
Record Date Created: 19980512
Record Date Completed: 19980512

4/7/16
DIALOG(R)File 155:MEDLINE(R)

11232088 98109428 PMID: 9449374
Characterization of the immune response after local delivery of recombinant adenovirus in murine pancreas and successful strategies for readministration.
McClane S J; Chirmule N; Burke C V; Raper S E
Institute for Human Gene Therapy and Harrison Department of Surgical Research, University of Pennsylvania School of Medicine, Philadelphia 19104, USA.
Human gene therapy (UNITED STATES) Dec 10 1997, 8 (18) p2207-16, ISSN 1043-0342 Journal Code: 9008950
Contract/Grant No.: 1F32DK09544-01; DK; NIDDK; DK 47757; DK; NIDDK
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The pancreas is an ideal organ for adenoviral gene therapy because of the high level of gene transfer that can be achieved and because of the many diseases that can potentially be treated using this technology. In this report, we characterize the immune response to direct pancreatic injection of adenovirus and we overcome some of the limitations it imposes by using immunosuppression. Direct injection of recombinant adenovirus into the pancreas leads to the production of neutralizing antibodies and to sensitized splenocytes which engage in increased cytotoxic, lymphoproliferative, and cytokine release activity when reexposed to adenovirus. Transgene expression is transient and the vector cannot be readministered. Deletion of CD4+ T helper cells improves expression over time (40% of pancreatic cells express transgene at day 28 vs. 5% in controls), and allows the vector to be readministered in the pancreas, albeit, inefficiently, when compared to naive animals. Similarly, blockade of CD40 ligand, which preserves the CD4+ T helper cell population, also improves expression over time (30% of pancreatic cells express transgene at day 28), and allows the vector to be readministered. With both approaches, neutralizing antibodies are decreased and the remaining splenocytes do not engage in activated immune responses. Thus, local delivery of the adenoviral vector induces a systemic response that prevents pancreatic readministration, even with direct injection. Blockade of CD40 ligand and T helper cell depletion are transient regimens that induce systemic immunosuppression. Until the development of newer strategies that selectively suppress adenoviral immune responses, these are viable alternatives for enhancement of pancreatic adenoviral delivery.
Record Date Created: 19980225
Record Date Completed: 19980225

4/7/17
DIALOG(R)File 155:MEDLINE(R)

11127323 98001376 PMID 9343211

An adenovirus-simian immunodeficiency virus env vaccine elicits humoral, cellular, and mucosal immune responses in rhesus macaques and decreases viral burden following vaginal challenge.

Buge S L; Richardson E; Alipanah S; Markham P; Cheng S; Kalyan N; Miller C J; Lubeck M; Udem S; Eldridge J; Robert-Guroff M

Basic Research Laboratory, National Cancer Institute, Bethesda, Maryland 20892, USA.

Journal of virology (UNITED STATES) Nov 1997, 71 (11) p8531-41, ISSN 0022-538X Journal Code: 0113724

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

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Six female rhesus macaques were immunized orally and intranasally at 0 weeks and intratracheally at 12 weeks with an adenovirus type 5 host range mutant (Ad5hr)-simian immunodeficiency virus SIVsm env recombinant and at 24 and 36 weeks with native SIVmac251 gp120 in Syntex adjuvant. Four macaques received the Ad5hr vector and adjuvant alone; two additional controls were naive. In vivo replication of the Ad5hr wild-type and recombinant vectors occurred with detection of Ad5 DNA in stool samples and/or nasal secretions in all macaques and increases in Ad5 neutralizing antibody in 9 of 10 macaques following Ad administrations. SIV-specific neutralizing antibodies appeared after the second recombinant immunization and rose to titers > 10,000 following the second subunit boost. Immunoglobulin G (IgG) and IgA antibodies able to bind gp120 developed in nasal and rectal secretions, and SIV-specific IgGs were also observed in vaginal secretions and saliva. T-cell proliferative responses to SIV gp140 and T-helper epitopes were sporadically detected in all immunized macaques. Following vaginal challenge with SIVmac251, transient or persistent infection resulted in both immunized and control monkeys. The mean viral burden in persistently infected immunized macaques was significantly decreased in the primary infection period compared to that of control macaques. These results establish in vivo use of the Ad5hr vector, which overcomes the host range restriction of human Ads for rhesus macaques, thereby providing a new model for evaluation of Ad-based vaccines. In addition, they show that a vaccine regimen using the Ad5hr-SIV env recombinant and gp120 subunit induces strong humoral, cellular, and mucosal immunity in rhesus macaques. The reduced viral burden achieved solely with an env-based vaccine supports further development of Ad-based vaccines comprising additional viral components for immune therapy and AIDS vaccine development.

Record Date Created: 19971113

Record Date Completed: 19971113

4/7/21

DIALOG(R)File 155:MEDLINE(R)

10338353 96140688 PMID: 8566039

Long-term humoral and cellular immunity induced by a single immunization with replication-defective adenovirus recombinant vector.

Juillard V; Villefroy P; Godfrin D; Pavirani A; Venet A; Guillet J G

Laboratoire d'Immunologie des Interactions Cellulaires et Moleculaires, INSERM Unite 152, Paris, France.

European journal of immunology (GERMANY) Dec 1995, 25 (12) p3467-73, ISSN 0014-2980 Journal Code: 1273201

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

This study examines the suitability of replication-defective adenovirus vectors for engineering recombinant vaccines. The immunological abilities and limitations of E1-deleted adenoviruses containing the lacZ gene (Ad-beta-gal) were investigated by examining the humoral and cellular immune responses to the beta-galactosidase protein. BALB/c mice (H-2d) were given in a single injection of recombinant adenovirus. The cytotoxic T lymphocyte (CTL) response of spleen cells was evaluated. Recognized target cells were H-2d-derived tumor cells transfected by the lac Z gene, or incubated with the 876-884 beta-galactosidase peptide known to be restricted by the Ld molecule of the major histocompatibility complex. A long-lasting beta-galactosidase-specific cytotoxic T cell response was obtained. By contrast, CTL from mice immunized with the Ld-restricted peptide were less specific for the endogenous epitope presented by the transfectants expressing beta-galactosidase. Ad-beta-gal-immunized mice were also protected against an intra-cerebral challenge with a recombinant vaccinia virus expressing the lac-Z gene. These results suggest that Ad-beta-gal-induced CTL have protective abilities in vivo. The induction of beta-galactosidase-specific T helper lymphocytes and humoral IgG responses were also examined. A proliferative response occurred only late after immunization and the primed T lymphocytes produced interleukin-2, but no interleukin-4. A humoral IgG response to the beta-galactosidase protein was detected 15-30 days after a single immunization and remained stable for 6 months without boosting. Lastly, we followed the evolution of the immune response over the course of successive immunizations. The magnitude and kinetics of the cellular and humoral responses were similar to those obtained after a single immunization. Consistent with these observations, an adenovirus-specific neutralizing antibody response was detected as early as the second immunization. Thus, a single immunization with a replication-defective adenovirus recombinant vector induces long-lasting humoral and cellular immune responses specific to the transgene product.

Record Date Created: 19960301

Record Date Completed: 19960301

4/7/26

DIALOG(R)File 155:MEDLINE(R)

09541383 21322033 PMID: 11429125

A conformational C4 peptide polymer vaccine coupled with live recombinant vector priming is immunogenic but does not protect against rectal SIV challenge.

Patterson L J; Robey F; Muck A; Van Remoortere K; Aldrich K; Richardson E ; Alvord W G; Markham P D; Cranage M; Robert-Guroff M
Basic Research Laboratory, National Cancer Institute, Bethesda, Maryland 20892, USA.

AIDS research and human retroviruses (United States) Jun 10 2001, 17 (9) p837-49, ISSN 0889-2229 Journal Code: 8709376
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The conserved, immunogenic CD4 binding site on the viral envelope is an attractive HIV or SIV vaccine candidate. Polymerization of an 18 amino acid segment derived from the C4 domain of SIV gp120 produced a peptide polymer or "peptomer," having an alpha-helical conformation possibly mimicking a proposed structure of the C4 domain in the unbound native protein. The SIV peptomer and native gp120 were compared as subunit boosts following two adenovirus type 5 host range (Ad5hr)-SIVenv recombinant priming immunizations. Both vaccine regimens successfully elicited SIV-specific CTL responses in five of six immunized macaques. Peptomer-boosted macaques exhibited significantly higher envelope-specific T cell proliferative responses than either the gp120-boosted macaques or controls. Peptomer immunization also elicited peptomer and SIV gp120-specific binding antibodies, but only native gp120 boosting elicited SIV neutralizing antibodies. Upon intrarectal challenge with SIVmac32H, all nine macaques became infected. The solely envelope-based vaccine conferred no protection. However, changing the boosting immunogen to the C4 peptomer did not improve protective efficacy in spite of its elicitation of humoral and cellular immune responses, including robust T-helper activity. In spite of the peptomer's strong immunogenicity and potential for induction of broadly protective immune responses, it was not effective as a subunit vaccine.

Record Date Created: 20010628
Record Date Completed: 20010927

4/7/32
DIALOG(R)File 155:MEDLINE(R)

09093523 20391204 PMID: 10933938

Role of vector in activation of T cell subsets in immune responses against the secreted transgene product factor IX.

Fields P A; Kowalczyk D W; Arruda V R; Armstrong E; McCleland M L; Hagstrom J N; Pasi K J; Ertl H C; Herzog R W; High K A
Department of Pediatrics, University of Pennsylvania Medical Center and The Children's Hospital of Philadelphia, 19104, USA.

Molecular therapy - the journal of the American Society of Gene Therapy (UNITED STATES) Mar 2000, 1 (3) p225-35, ISSN 1525-0016
Journal Code: 100890581
Contract/Grant No.: RO1 HL611921; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
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Defining immune responses against the secreted transgene product in a gene therapy setting is critical for treatment of genetic diseases such as hemophilia B (coagulation factor IX deficiency). We have previously shown that intramuscular administration of an adeno-associated viral (AAV) vector results in stable expression of therapeutic levels of factor IX (F.IX) and may be associated with humoral immune responses against F.IX. This study demonstrates that intramuscular injection of an AAV vector expressing F.IX fails to activate F.IX-specific cytotoxic T lymphocytes (CTLs) in hemostatically normal or in hemophilia B mice, so that there is an absence of cellular immune responses against F.IX. However, transgene-derived F.IX can cause B cell responses characterized by production of T helper cell-dependent antibodies (predominantly IgG1, but also IgG2 subclasses) resulting from activation of CD4+ T helper cells primarily of the Th2 subset. In contrast, administration of an adenoviral vector efficiently activated F.IX-specific CTLs and T helper cells of both Th1 and Th2 subsets, leading to inflammation and destruction of transduced muscle tissue and activation of B cells as well. Therefore, vector sequences fundamentally influence T cell responses against transgene-encoded F.IX. In conclusion, activation of the immune system in AAV-mediated gene transfer is restricted to pathways mediated by F.IX antigen presentation through MHC class II determinants resulting in T and B cell responses that are more comparable to responses in the setting of protein infusion rather than of viral infection/gene transfer.

Record Date Created: 20000901
Record Date Completed: 20000901

4/7/36
DIALOG(R)File 155:MEDLINE(R)

08790590 20072754 PMID: 10605018

Th2-dependent B cell responses in the absence of CD40-CD40 ligand interactions.

Chirmule N; Tazelaar J; Wilson J M
Institute for Human Gene Therapy, Department of Molecular Engineering, University of Pennsylvania, Philadelphia 19104, USA.

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Jan 1 2000, 164 (1) p248-55, ISSN 0022-1767 Journal Code: 2985117R
Contract/Grant No · P30 DK47757-04, DK, NIDDK, R01 HL49040-06, HL, NHLBI

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

CD40 is thought to play a central role in T cell-dependent humoral responses through two distinct mechanisms. CD4+ T helper cells are activated via CD40-dependent Ag presentation in which CD80/CD86 provides costimulation through CD28. In addition, engagement of CD40 on B cells provides a direct pathway for activation of humoral responses. We used a model of adenovirus-mediated gene transfer of beta-galactosidase (lacZ) into murine lung to evaluate the specific CD40-dependent pathways required for humoral immunity at mucosal surfaces of the lung. Animals deficient in CD40L failed to develop T and B cell responses to vector. Activation of Th2 cells, which normally requires CD40-dependent stimulation of APCs, was selectively reconstituted in CD40 ligand-deficient mice by systemic administration of an Ab that is agonistic to CD28. Surprisingly, this resulted in the development of a functional humoral response to vector as evidenced by formation of germinal centers and production of antiadenovirus IgG1 and IgA that neutralized and prevented effective readministration of vector. The CD28-dependent B cell response required CD4+ T cells and was mediated via IL-4. These studies indicate that CD40 signals to the B cells are not necessary for CD4+ Th2 cell-dependent humoral responses to be generated.

Record Date Created: 20000119
Record Date Completed: 20000119

4/7/38
DIALOG(R)File 155:MEDLINE(R)

08747112 20027252 PMID: 10559341

Adenoviruses activate human dendritic cells without polarization toward a T-helper type 1-inducing subset.

Rea D; Schagen F H; Hoeben R C; Mehtali M; Havenga M J; Toes R E; Melief C J; Offringa R

Department of Immunohematology, Leiden University Medical Center, 2300 RC Leiden, The Netherlands. D.G.Rea@Immunohematology.Medfac.Leidenuniv.nl

Journal of virology (UNITED STATES) Dec 1999, 73 (12) p10245-53, ISSN 0022-538X Journal Code: 0113724

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Human monocyte-derived dendritic cells (DC) infected with recombinant adenoviruses (rAd) are promising candidate vaccines for inducing protective immunity against pathogens and tumors. However, since some viruses are known to negatively affect DC function, it is important to investigate the interactions between rAd and DC. We now show that infection by rAd enhances the immunostimulatory capacity of immature human monocyte-derived DC through the upregulation of the costimulatory molecules CD80, CD86, and CD40 and the major histocompatibility complex class I and II molecules. Although rAd infection fails to induce the secretion of interleukin-12 (IL-12) and only marginally induces the expression of the DC maturation marker CD83, it acts in synergy with CD40 triggering in rendering DC fully mature. rAd-infected DC triggered through CD40 produce more IL-12 and are more efficient in eliciting T-helper type 1 responses than DC activated by CD40 triggering only. rAd lacking one or more of the early regions, E1, E2A, E3, and E4, which play an important role in virus-host cell interactions are equally capable of DC activation. Efficient DC infection requires a high multiplicity of infection (>1,000), a fact which can be attributed to the absence of the coxsackievirus and adenovirus receptor on this cell type. Despite the poor ability of DC to be infected by rAd, which may be improved by targeting rAd to alternative DC surface molecules, DC infected with all currently tested rAd constitute potent immunostimulators. Our study provides new insights into the interactions between two highly promising vaccine components, rAd and DC, and indicates that their combination into one vaccine may be very advantageous for the stimulation of T-cell immunity.

Record Date Created: 19991220
Record Date Completed: 19991220

4/7/42
DIALOG(R)File 155:MEDLINE(R)

08502692 95190968 PMID: 7884845

Cellular and humoral immune responses to viral antigens create barriers to lung-directed gene therapy with recombinant adenoviruses.

Yang Y; Li Q; Ertl H C; Wilson J M

Institute for Human Gene Therapy, University of Pennsylvania Medical Center, Philadelphia 19104.

Journal of virology (UNITED STATES) Apr 1995, 69 (4) p2004-15, ISSN 0022-538X Journal Code: 0113724

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Recombinant adenoviruses are an attractive vehicle for gene therapy to the lung in the treatment of cystic fibrosis (CF). First-generation viruses deleted of E1a and E1b transduce genes into airway epithelial cells in vivo; however, expression of the transgene is transient and associated with substantial inflammatory responses, and gene transfer is significantly reduced following a second administration of the virus. In this study, we have used mice deficient in immunological effector functions in combination with adoptive and passive transfer techniques to define antigen-specific cellular and humoral immune responses that underlie these important

limitations. Our studies indicate that major histocompatibility complex class I-restricted CD8+ cytotoxic T lymphocytes are activated in response to newly synthesized antigens, leading to destruction of virus infected cells and loss of transgene expression. Major histocompatibility complex class II-associated presentation of exogenous viral antigens activates CD4+ T-helper (TH) cells of the TH1 subset and, to a lesser extent, of the TH2 subset. CD4+ cell-mediated responses are insufficient in the absence of cytotoxic T cells to completely eliminate transgene containing cells; however, they contribute to the formation of neutralizing antibodies in the airway which block subsequent adenovirus-mediated gene transfer. Definition of immunological barriers to gene therapy of cystic fibrosis should facilitate the design of rational strategies to overcome them.
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Record Date Completed: 19950410
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S3 6 S1 AND S2
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DIALOG(R)File 155:MEDLINE(R)
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07502842 92366545 PMID: 1502197
Adenovirus-human immunodeficiency virus (HIV) envelope recombinant vaccines elicit high-titered HIV-neutralizing antibodies in the dog model.
Natuk R J; Chanda P K; Lubeck M D; Davis A R; Wilhelm J; Hjorth R; Wade M S; Bhat B M; Mizutani S; Lee S; et al
Department of Biotechnology, Wyeth-Ayerst Research, Philadelphia, PA 19101.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Aug 15 1992, 89 (16) p7777-81, ISSN 0027-8424
Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Recombinant human adenoviruses (Ads) (types 4, 5, and 7) expressing the HIV-1 envelope membrane glycoprotein (gp160) were tested for immunogenicity in the dog. Administration of recombinant Ad7-env by intratracheal inoculation resulted in a low serum antibody response to gp160, which developed over several weeks. A strong neutralizing antibody response to the Ad7 vector developed within 1 week of infection. A subsequent booster inoculation 12 weeks later with the heterotypic Ad4-env recombinant virus resulted in significantly enhanced humoral responses directed at the envelope antigen, as measured by both ELISA and Western blot analysis as well as high-titer type-specific neutralizing antibodies, with some animals achieving neutralization titers approaching 1000. Recombinant HIV envelope glycoprotein derived from Ad-HIV-infected cell cultures was used as a subunit booster injection for dogs that had previously received sequential immunizations with heterotypic recombinant Ads. Significant immune responses against the envelope developed as measured by ELISA, Western blot analysis, and neutralization assays. These data indicate that live recombinant Ad-HIV vaccines are capable of inducing high-titer type-specific neutralizing antibodies to gp160 in vivo. Recombinant HIV envelope glycoprotein subunit vaccines, prepared from Ad-env-infected cells, are capable of boosting these responses.
Record Date Created: 19920915
Record Date Completed: 19920915

3/7/2
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
08358974 95046945 PMID: 7958485
Adenovirus vectored vaccines.
Natuk R J; Davis A R; Chanda P K; Lubeck M D; Chengalvala M; Murthy S C; Wade M S; Dheer S K; Bhat B M; Murthy K K; et al
Wyeth-Ayerst Research, Biotechnology & Microbiology Division, Philadelphia, PA

Developments in biological standardization (SWITZERLAND) 1994, 82 p71-7, ISSN 0301-5149 Journal Code: 0427140
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Human recombinant adenoviruses (Ad) have been employed to develop experimental vaccines against a number of infectious agents. Ad-vectored vaccines express recombinant proteins, including any post-translational modifications, into functioning replicas of the native proteins capable of eliciting neutralizing antibodies in both abortive and permissive animal models. Human Ad types 4, 5, and 7 were used to construct recombinant viruses that express the respiratory syncytial virus F or G glycoproteins, the hepatitis B surface antigen, and the HIV env or gag genes. The recombinant Ad-HIV viruses are of particular interest and have been examined for their immunogenicity in dogs and chimpanzees. Dogs were immunized intratracheally with Ad-env recombinants (10(9) pfu/dog). Excellent humoral anti-HIV responses, including neutralizing antibodies, were detected in the sera following booster immunization (12-18 weeks after primary immunization) with a second Ad-env recombinant made in a different Ad serotype (heterotypic booster). Chimpanzees were immunized in two ways, orally with lyophilized virus (10(9) to 10(10) pfu/virus) in enteric-coated capsules or intranasally (10(7) pfu/virus). Intranasal immunization was superior to oral immunization with respect to replication of recombinant viruses as well as induction of anti-Ad and anti-HIV antibodies. Administration by both routes resulted in stimulation of cellular immune responses, as measured by antigen proliferation assays. Anti-HIV antibodies were detected in chimpanzee secretions (salivary, nasal, rectal, vaginal) taken from animals following intranasal immunization with a heterotypic recombinant. Intranasal administration effectively primed chimpanzees to produce high-titred (320-640) serum neutralizing antibodies to HIV following boosting with a baculovirus-derived env (gp160) subunit vaccine.(ABSTRACT TRUNCATED AT 250 WORDS)
Record Date Created: 19941221
Record Date Completed: 19941221

3/7/1
DIALOG(R)File 155:MEDLINE(R)

10966902 97319589 PMID: 9176492
Long-term protection of chimpanzees against high-dose HIV-1 challenge induced by immunization.
Lubeck M D; Natuk R; Myagkikh M; Kalyan N; Aldrich K; Sinangil F; Alipanah S; Murthy S C; Chanda P K; Nigida S M; Markham P D; Zolla-Pazner S ; Steimer K; Wade M; Reitz M S; Arthur L O; Mizutani S; Davis A; Hung P P; Gallo R C; Eichberg J; Robert-Guroff M
Wyeth-Ayerst Research, Radnor, PA 19087, USA.
Nature medicine (UNITED STATES) Jun 1997, 3 (6) p651-8, ISSN 1078-8956 Journal Code: 9502015
Contract/Grant No.: AI 32424; AI; NIAID; AI 36085; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A combination AIDS vaccine approach consisting of priming with adenovirus-HIV-1MN gp160 recombinants followed by boosting with HIV-1SF2 gp120 was evaluated in chimpanzees. Long-lasting protection, requiring only three immunizations, was achieved against a low-dose challenge with the SF2 strain of HIV-1 and a subsequent high-dose SF2 challenge administered 1 year later without an intervening boost. Notably, neutralizing antibody responses against both clinical and laboratory isolates developed in three chimpanzees and persisted until the time of high-dose challenge. The possibility that cytotoxic T-lymphocytes contribute to low-dose protection of a chimpanzee lacking neutralizing antibodies is suggested. Our results validate the live vector priming/subunit booster approach and should stimulate interest in assessing this combination vaccine approach in humans.
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